

University of Groningen

## Value of Information Analysis from a Societal Perspective

Mohseninejad, Leyla; van Baal, Pieter H. M.; van den Berg, Matthijs; Buskens, Erik; Feenstra, Talitha

*Published in:*  
Value in Health

*DOI:*  
[10.1016/j.jval.2012.12.007](https://doi.org/10.1016/j.jval.2012.12.007)

**IMPORTANT NOTE:** You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2013

[Link to publication in University of Groningen/UMCG research database](#)

### *Citation for published version (APA):*

Mohseninejad, L., van Baal, P. H. M., van den Berg, M., Buskens, E., & Feenstra, T. (2013). Value of Information Analysis from a Societal Perspective: A Case Study in Prevention of Major Depression. *Value in Health*, 16(4), 490-497. <https://doi.org/10.1016/j.jval.2012.12.007>

### **Copyright**

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### **Take-down policy**

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

*Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.*

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

SciVerse ScienceDirect

journal homepage: [www.elsevier.com/locate/jval](http://www.elsevier.com/locate/jval)

## ORIGINAL RESEARCH Economic Evaluation

# Value of Information Analysis from a Societal Perspective: A Case Study in Prevention of Major Depression

Leyla Mohseninejad, MSc<sup>1,\*</sup>, Pieter H. M. van Baal, PhD<sup>2</sup>, Matthijs van den Berg, PhD<sup>3</sup>, Erik Buskens, PhD<sup>1</sup>, Talitha Feenstra, PhD<sup>1,4</sup>

<sup>1</sup>Department of Epidemiology, Unit Health Technology Assessment, University Medical Center Groningen, The University of Groningen, Groningen, The Netherlands; <sup>2</sup>Expertise Centre for Methodology and Information Services, National Institute for Public Health and the Environment, Bilthoven, The Netherlands; <sup>3</sup>Centre for Public Health Forecasting, National Institute of Public Health and the Environment, Bilthoven, The Netherlands; <sup>4</sup>Department of Prevention and Health Services Research, National Institute for Public Health and the Environment, Bilthoven, The Netherlands

## ABSTRACT

**Objectives:** Productivity losses usually have a considerable impact on cost-effectiveness estimates while their estimated values are often relatively uncertain. Therefore, parameters related to these indirect costs play a role in setting priorities for future research from a societal perspective. Until now, however, value of information analyses have usually applied a health care perspective for economic evaluations. Hence, the effect of productivity losses has rarely been investigated in such analyses. The aim of the current study therefore was to investigate the effects of including or excluding productivity costs in value of information analyses. **Methods:** Expected value of information analysis (EVPI) was performed in cost-effectiveness evaluation of prevention from both societal and health care perspectives, to give us the opportunity to compare different perspectives. Priorities for future research were determined by partial EVPI. The program to prevent major depression in patients with subthreshold depression was

opportunistic screening followed by minimal contact psychotherapy. **Results:** The EVPI indicated that regardless of perspective, further research is potentially worthwhile. Partial EVPI results underlined the importance of productivity losses when a societal perspective was considered. Furthermore, priority setting for future research differed according to perspective. **Conclusions:** The results illustrated that advice for future research will differ for a health care versus a societal perspective and hence the value of information analysis should be adjusted to the perspective that is relevant for the decision makers involved. The outcomes underlined the need for carefully choosing the suitable perspective for the decision problem at hand. **Keywords:** cost-effectiveness, perspective, productivity costs, uncertainty, value of information analysis.

Copyright © 2013, International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc.

## Introduction

Estimates of cost-effectiveness are surrounded by uncertainty. Reduction of uncertainty is usually costly. A value of information (VOI) analysis estimates the monetary value of investments that may be required to eliminate all or part of uncertainty in the evaluations. Such estimation can support the decision maker in deciding whether further research is warranted [1]. When further research turns out to be worthwhile, more detailed VOI analysis can identify the uncertainties that should then become research priorities. VOI for parameters estimates the expected VOIs on groups of parameters and assists the decision maker to decide on those uncertainties. The concept of VOI analysis [1] was applied in many sectors [2] before it was introduced in health technology assessment by Claxton [3]. Recently, the number of applications in health care has steadily grown. A range of studies was published after 2004 [4–13].

While the societal perspective is recommended for economic evaluations in many countries [14], the majority of the previous studies have applied a health care perspective in analyzing the VOI. Studies performed in the United Kingdom were just following national directives in adopting a health care perspective according to The Guidelines Manual [15]. Also, among the non-UK studies, however, only a few have taken into account other than direct health care costs. Some included direct non-health care or some part of indirect health care costs [10,16]; however, they have ignored productivity losses. Galani et al. [17] mentioned that cost estimates included indirect costs, but they did not elaborate further on the consequences of this for the interpretation of their results. Nevertheless, most guidelines that recommend using a societal perspective also suggest comparing the results from two perspectives. Such a comparison has been usually missing from the studies. The review by Yokota and Thompson [2] highlights that in other sectors

\* Address correspondence to: Leyla Mohseninejad, P.O. Box 30.001, Hanzeplein 1, 9700 RB Groningen, The Netherlands.

E-mail: [l.mohseninejad@umcg.nl](mailto:l.mohseninejad@umcg.nl).

also applications have often chosen a relatively narrow perspective. Hence, to the best of our knowledge, only very few articles have included productivity losses and if they did, the implications were not thoroughly discussed. This seems an omission because in interventions that target chronic diseases with a high prevalence among patients in their working ages, productivity costs may have a large impact on cost-effectiveness results. Furthermore, productivity costs often can be estimated only with large uncertainty. Information on individuals' working hours as well as hourly productivity may be difficult to ascertain and is not often included in most clinical trials. Therefore, looking at the impact of the choice of perspective and inclusion of productivity costs on the outcomes of a VOI analysis is worthwhile and was the aim of the current study.

A case study was chosen in the field of mental disorders. Many reports show that mental disorders lead to a reduction in employee productivity due to absenteeism or impaired functioning at work [18]. Depression is one of the major mental disorders with a high burden of disease [19,20]. Because of work loss, absenteeism, and presentism, productivity losses resulting from depression are considerable [21]. A recent study showed that productivity costs, on average, reflect more than half of the total costs for the treatment of depressive disorders [22]. In fact, the majority of costs of depression fall outside the health care sector; that is, the benefits of preventing depression are not restricted to the health sector but society as a whole. Accordingly, for many health care decision makers it will be relevant to consider a societal perspective in addition to the health care perspective in evaluating cost-effectiveness in depression prevention. Still, to date, most economic evaluations of treatments for adults with depressive disorders have ignored productivity losses [22].

The objective of our study then was to perform a VOI analysis in cost-effectiveness evaluation of preventing major depression (MD) in patients with minor depression. We considered both a societal and a health care perspective and paid attention to the consequences of different perspectives for policy advice. The depression case serves as an illustration for many interventions with large but uncertain effects on productivity costs.

## Materials and Methods

In a recent study [23], a Markov model based on Vos et al. [24] was used to evaluate the costs and long-term health benefits of screening followed by minimal contact psychotherapy (MCP) for depression prevention. The model was adjusted to allow evaluation of depression prevention and was adapted to the Dutch setting. The short-term outcomes of MCP were previously evaluated alongside a randomized controlled trial [21]. The current article adds an elaborate VOI analysis and focuses on a comparison between the values of solving uncertainties for different perspectives. The model was used to extrapolate the trial outcomes over a 5-year time horizon. Five years were considered long enough to capture the full effects of the intervention and still short enough to trust the data on the population and the screening results. The discount rates used were 1.5% and 4% according to the Dutch Guidelines for pharmacoeconomic research [25], and monetary outcomes were valued in euros, at the 2008 price level. For clarity reasons, we explain the intervention, the model, and parameter estimation sources in the following sections.

### Intervention

The intervention was opportunistic screening for subthreshold depression followed by MCP. Full details about the intervention and its short-term effects compared with no screening have been published before [26]. In short, opportunistic screening takes place in three steps: first, people are approached by the assistant when they are in the waiting room during a regular general

practitioner visit. Those who are eligible for screening and give informed consent (participation rate 72.5%) are then screened for subthreshold depression (screen positive rate 26.6%). In a second step, screen-positive patients are approached for a further screening to check whether they meet the inclusion criteria for subthreshold depression (participation rate 35.7%). Those who meet all inclusion criteria receive MCP (59.5% of positive screens).

MCP consists of a self-help manual with instructions on cognitive-behavioral self-help in mood management skills. The manual contains registration exercises and homework assignments aimed at cognitive restructuring, relaxation, and activity scheduling to increase pleasant activities.

In the control group, no screening took place. People with subthreshold depression received care as usual from their general practitioner; that is, they were offered treatment on presenting themselves with symptoms.

The effects of the intervention were twofold: incidence and recurrence of MD decreased by 6% [26] and the total annual per-capita costs decreased by 21% [21].

### Patient Population

The intervention targets patients with minor (subthreshold) depression. Subthreshold depression, which is diagnosed when a patient has two to four symptoms of MD, has a lifetime prevalence of 10% [27]. People with minor depression have an increased risk of developing MD compared with those not meeting the criteria of subthreshold depression [28].

### Markov Model

The model distinguishes three main states: subthreshold depression, MD, and recovered from depression (no MD). Each state is divided into episodes that last for 4 weeks. After each cycle of 4 weeks, a person has the chance of moving to another state of disease, or to stay in the same state and start a new episode within that state. The Markov model is depicted in Figure 1.

The probability of developing MD for people with subthreshold depression (the incidence rate) has been assumed to be independent of the time that persons were in the subthreshold state, while the probabilities of recovery from MD and relapse into MD by assumption decreased over the time that was spent in MD and no-MD states, respectively. Parameters related to costs and quality-adjusted life-years (QALYs) in the recovered states are by assumption the same as in the subthreshold states.

Modeling and analyses were all done by means of the R software environment for statistical computing.

### Parameter Estimation

Estimates of relapse and recovery rate as a function of duration were based on the Dutch NEMESIS study [19], a large population-based cohort study addressing mental disorders. The time-dependent probability curves for relapse and recovery rates can be found in van den Berg et al. [23]. Prevalence of subthreshold depression, intervention costs, and health care and societal costs for subthreshold depression were based on trial results [21]. Population parameters and incidence probabilities from subthreshold depression to MD were taken from Willemse et al. [26]. Costs and productivity losses for MD were estimated on the basis of a review of Dutch studies [29–31]. QALY estimates were based on the NEMESIS study [19]. Distribution functions were estimated for all important model parameters. Parameters that were used in the probabilistic sensitivity analysis are presented in Table 1.

Effects of MCP were conservatively assumed to cease 1 year after the intervention. That is, after 1 year, persons are assumed to return to the same risk of developing MD as under care as usual if still in the subthreshold state.

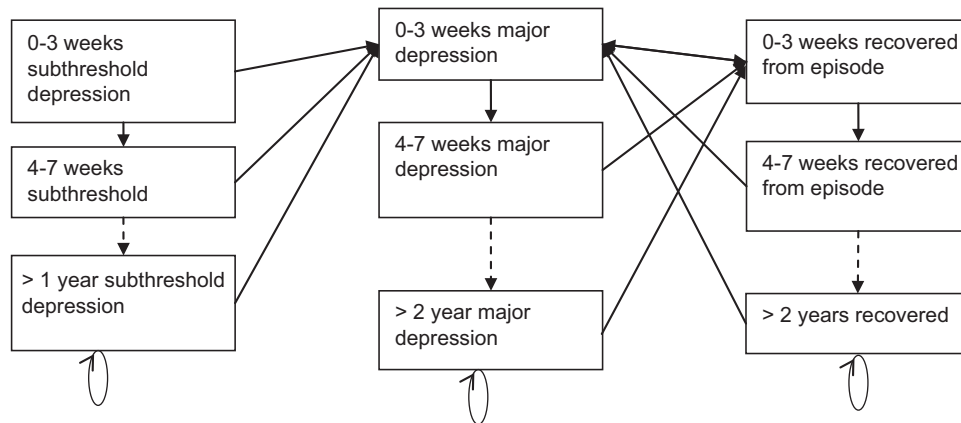


Fig. 1 – The Markov Model.

### Expected Value of Perfect Information

The expected value of perfect information (EVPI) was calculated for a cost-effectiveness range of 0 to 60,000 €/QALY. The global EVPI was computed as the difference between the expected net benefit of perfect and current information over a sufficient number of simulations, and the net benefits of the standard therapy (no MCP) were assumed to be zero:

$$EVPI = E_{\theta} \max[0, NB(MCP, \theta)] - \max[E_{\theta} NB(MCP, \theta), 0]$$

Here  $\theta$  represents a list of unknown parameters. Population EVPIs were then computed by multiplying global EVPIs by the relevant population sizes. These were based on the prevalence of subthreshold depression [21].

In addition to this, parameters were grouped to find the expected value of perfect parameter information (EVPII) for each of these groups of parameters. EVPII or partial EVPI is intended to inform research priorities, that is, the type of additional evidence that would be the most valuable to inform the decision. Parameters that explained the same concepts were grouped together, as shown in Table 1. Like the global EVPI, the partial EVPIs were analyzed for different cost-effectiveness thresholds to see how they varied for a range of thresholds.

The EVPII is calculated as the difference between the expected value of a decision made with perfect information on a group of parameters and the expected value with current information on that group of parameters. It reflects the maximum value of additional information on the value of this group of parameters and may serve to help decide whether certain research to find better information on the parameters is worth its costs:

$$EVPII_{\phi} = E_{\phi} \max[0, E_{\psi|\phi}(MCP, \phi, \psi)] - \max[E_{\theta} NB(MCP, \theta), 0]$$

where  $\phi$  is the group of parameters of interest and  $\psi$  represents the remaining uncertain parameters. To compute the partial EVPI, first the simulation must be run for parameters  $\psi$  but with a particular value of  $\phi$  (an inner loop) and then a new value of  $\phi$  is sampled and the simulation is run again (an outer loop). This process is repeated until we have sampled sufficiently from the distribution of  $\phi$  [32].

### Number of Simulations

Careful selection of the number of simulations needed in the inner and outer loops is required to balance off computation time and precision. The number of sufficient inner and outer loops for the EVPII was computed by using a three-stage algorithm that

estimates the bias and confidence intervals for the outcomes of EVPII [33]. Predicted bias and the width of 95% confidence intervals for different number of inner loops ( $J$ ) and outer loops ( $K$ ) are presented in Table 2 for the health care perspective. The numbers presented are relative values, indexing the global EVPI (43,500,000 €) to 100. We chose  $J = 1000$  and  $K = 100$  as the sufficient numbers for our simulation from both perspectives because the bias was reasonably low and also the width of the confidence interval was estimated to be low enough at 3% of the global EVPI.

## Results

Estimates of effects and costs per intervention together with incremental effects and costs are shown in Table 3. From a health care perspective, the incremental cost-effectiveness ratio of MCP compared with the standard therapy (no MCP) is about 1100 €/QALY. From a societal perspective, the intervention is cost saving [23].

We illustrate our results showing outcomes for two different perspectives in single pictures/graphs with the cost-effectiveness threshold on the horizontal axis, allowing a comparison of the societal and health care perspectives.

### EVPI

Figure 2 depicts the cost-effectiveness acceptability curves (CEACs) together with results of EVPI from a societal perspective and a health care perspective. CEACs were also presented by van den Berg et al. [23], but are repeated here to support explanation of the EVPI.

From a health care perspective, at low cost-effectiveness thresholds, prevention by using MCP is not cost-effective. The value of perfect information is relatively low because the decision not to implement MCP is relatively certain to be the best decision. The EVPI rises to a maximum of 57 million euros at a threshold value of about 1100 €/QALY, which is equal to the mean cost-effectiveness of the intervention from a health care perspective. For larger thresholds, the probability that the MCP is cost-effective increases and the EVPI decreases with the threshold rising. At a threshold surpassing the mean incremental cost-effectiveness ratio, we expect the intervention to be cost-effective and the decision is less likely to be changed by further information. With increasing cost-effectiveness thresholds, the value paid for each additional QALY increases. Hence, at high

**Table 1 – Distributions of the parameters of intervention used in PSA (the EVPPI group indicates how the parameters were grouped for the partial value of information analysis).**

		No MCP		MCP		EVPPI group
		Distribution	Mean (SE)	Distribution	Mean (SE)	
Screening process	Fraction of the target population that agrees to be screened [26]			Beta distribution ( $\alpha = 3826$ ; $\beta = 1452$ )	0.725 (0.006)	Population
	Fraction of screened included for diagnostic interview [26]			Beta distribution ( $\alpha = 364$ ; $\beta = 3463$ )	0.095 (0.005)	Population
	Fraction of interviewed included in intervention [26]			Beta distribution ( $\alpha = 217$ ; $\beta = 148$ )	0.595 (0.026)	Population
Subthreshold states	Incidence probabilities from subthreshold to major depression [26]	Beta distribution ( $\alpha = 21$ ; $\beta = 90$ )	0.016 (0.003)	Beta distribution ( $\alpha = 14$ ; $\beta = 95$ )	0.011 (0.003)	Incidence rate
	Health care costs [21]	Gamma distribution (shape = 15; scale = 108)	1627 (419)	Gamma distribution (shape = 31; scale = 55)	1687 (305)	Health care costs subthreshold
	Productivity loss [21]	Gamma distribution (shape = 22; scale = 300)	6481 (1393)	Gamma distribution (shape = 8; scale = 576)	4638 (1634)	Productivity loss
	Direct nonmedical costs [21]	Gamma distribution (shape = 43; scale = 12)	507 (77)	Gamma distribution (shape = 56; scale = 8)	441 (59)	–
	Quality of life [19]	Uniform distribution (0.81–1)	0.91 (0.05)	Same as no MCP		QALYs
Major depression states	Health care costs [29–31]	Gamma distribution (shape = 15; scale = 152)	2280 (589)	Same as no MCP		Health care costs major depression
	Productivity loss [29–31]	Gamma distribution (shape = 8; scale = 27)	216 (76)	Same as no MCP		Productivity loss

EVPPI, expected value of perfect parameter information; MCP, minimal contact psychotherapy; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life-years; SE, standard error.



**Table 2 – Predicted bias and 95% CI for Monte Carlo partial EVPI estimate [33], EVPI indexed to 100.**

	<i>J</i> = 10	<i>J</i> = 100	<i>J</i> = 500	<i>J</i> = 1,000	<i>J</i> = 5,000	<i>J</i> = 10,000
Bias (independent of <i>K</i> )	7.62	−0.54	−0.21	−0.05	0.03	−0.09
95% CI						
<i>K</i> = 10	303.74	56.63	24.82	17.95	11.1	5.2
<i>K</i> = 100	35.94	10.14	4.5	2.94	1.51	0.83
<i>K</i> = 500	7.16	2.02	0.9	0.59	0.3	0.17
<i>K</i> = 1,000	3.58	1.01	0.45	0.29	0.15	0.08
<i>K</i> = 5,000	0.72	0.2	0.1	0.06	0.03	0.02
<i>K</i> = 10,000	0.35	0.1	0.05	0.03	0.01	0.01

CI, confidence interval; EVPI, expected value of perfect information.

**Table 3 – Estimates of effects and costs per intervention and incremental effects and costs.**

	QALYs ×(1,000)	Health care costs ×(1,000,000)	Total costs ×(1,000,000)
No MCP	1,158	2,911	11,612
MCP	1,170	2,924	11,240
Incremental	12	13	−372

MCP, minimal contact psychotherapy; QALY, quality-adjusted life-year.

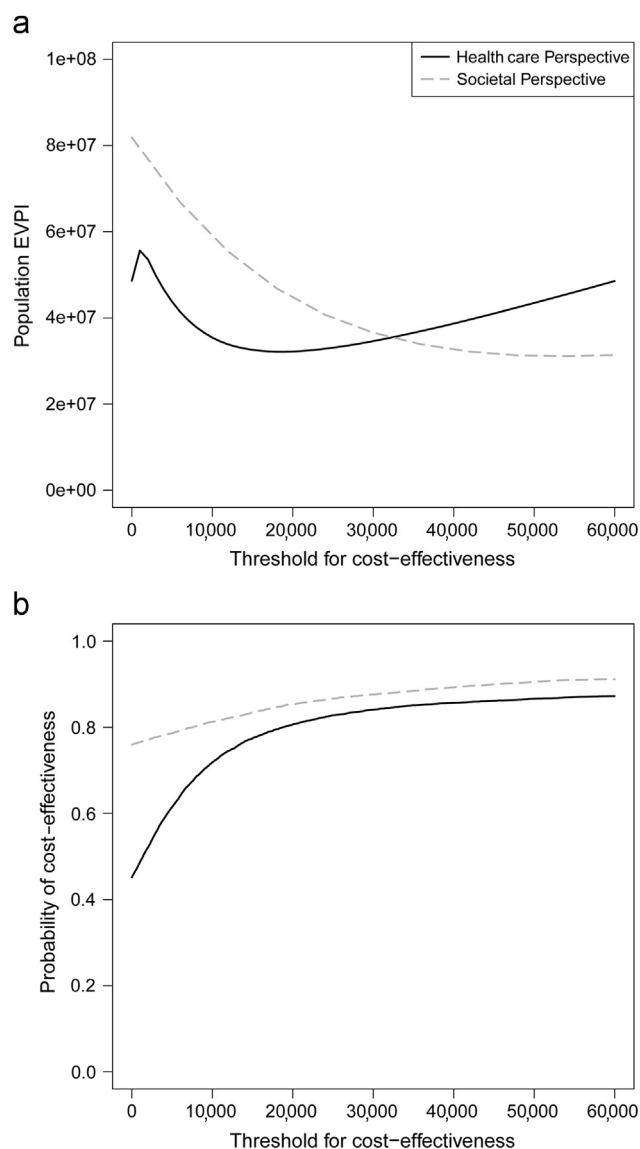
values of the threshold, the global EVPI rises again because of an increased investment risk.

In contrast, from a societal perspective, the intervention is cost saving on average and the probability of a correct decision is always increasing as the threshold gets higher; hence, the global EVPI is always decreasing. We expect, however, that at very high thresholds (which are not shown in these graphs), the EVPI starts to rise, because high threshold values mean that a wrong decision is extremely costly.

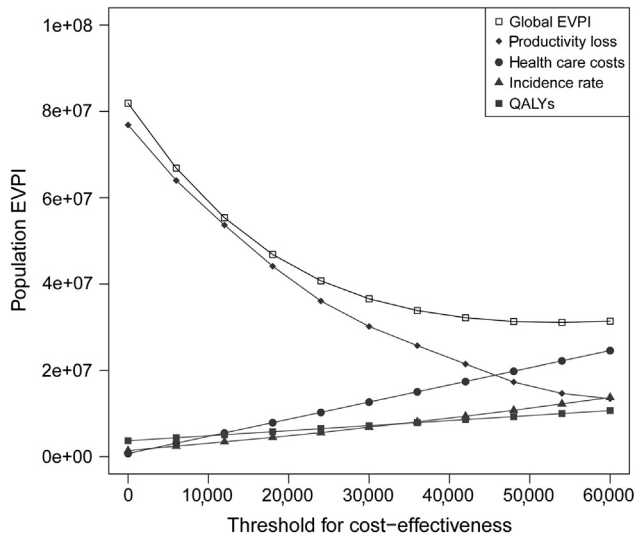
It is apparent that the VOI is mostly higher from a societal perspective than from a health care perspective. Toward the right end of the willingness-to-pay scale, however, the VOI from the health care perspective rises above the levels of the EVPI from a societal perspective. This can be explained by having a look at the CEAC: it shows that the probability of making an incorrect decision remains higher for the health care perspective. Comparisons, however, of the VOI for different perspectives might require different willingness-to-pay thresholds. The amount that the decision maker is willing to pay per additional QALY would most likely change when different perspectives are considered. Therefore, to reach the best comparison, the values of the thresholds relevant for the decision makers should be known. For instance, if the threshold for evaluating MCP from a health care perspective is 20,000 €/QALY and the threshold for the same intervention from a societal perspective is 40,000 €/QALY, then the CEACs and EVPIs must be compared on two different points of 20,000 and 40,000 €/QALY on the x-axis. The vertical lines in Figure 2 show the comparison considering these hypothetical threshold values. We will come back to this point in discussion.

### Partial EVPI

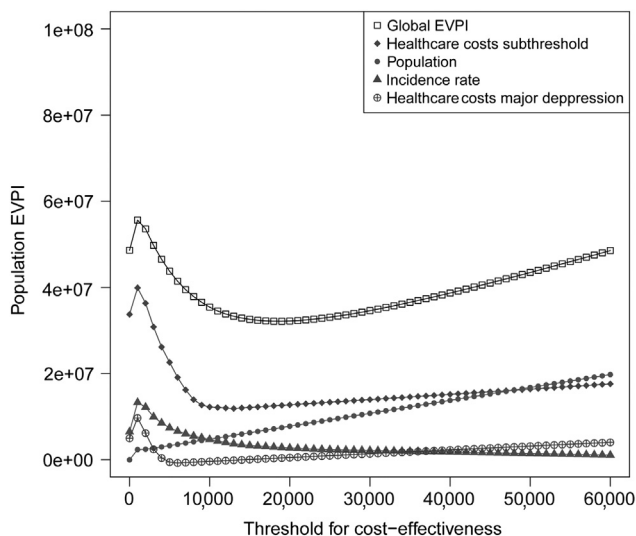
The EVPI for separate parameters groups from the societal perspective is illustrated in Figure 3. Results indicated that when the societal perspective is considered, the productivity loss was the most important source of uncertainty at any threshold. The effect of productivity loss, however, was more important for low

**Fig. 2 – (a) Global expected value of perfect information (EVPI) curves; and (b) Cost effectiveness acceptability curves.**

thresholds than for higher ones. The next important parameter group was health care costs (including both subthreshold depression and MD), which became more prominent at higher thresholds. The third and fourth priorities would be given to parameters related to QALYs and the incidence rate. Other parameters, such



**Fig. 3 – Partial EVPI curves considering a societal perspective. EVPI, expected value of perfect information; QALY, quality-adjusted life-year.**



**Fig. 4 – Partial EVPI curves considering a health-care perspective. EVPI, expected value of perfect information.**

as population and recovery-relapse rates, were not significantly affecting the VOI, indicating that they would have a low priority in further research.

Results of the partial EVPI from a health care perspective are shown in Figure 4.

The partial EVPI graph indicated that the most important sources of uncertainty were health care costs. Because health care costs had such a clear effect on the uncertainty of the problem, they have been subdivided into two groups of parameters: health care costs in subthreshold depression and in MD. At very low thresholds, costs of MD were more important than at high thresholds. The health care costs of MD had an almost negligible expected VOI at thresholds above 5000 €/QALY. The incidence rate also had a considerable impact at low thresholds, but a low impact at high thresholds. Results showed that the most important priorities in future research were those related to

the health care costs of subthreshold depression. The population that will finally receive the MCP also became an important parameter at high willingness-to-pay thresholds. This parameter is determined by the fraction of the target population that agrees to be screened, fraction of screened included for diagnostic interview, and fraction of interviewed included in intervention. Other parameters, related to QALYs, recovery rates, and relapse rates, were of very little importance in the health care perspective.

## Discussion

This article examined how the VOI would change for different perspectives. The case study was the decision whether to use opportunistic screening in combination with MCP to reduce the incidence of MD. For depression, absence from work and the associated productivity costs represent an important part of the burden of disease. For this reason, results were evaluated both from a societal perspective and from a health care perspective. We found that regardless of the perspective, parameters related to costs had the largest EVPIs; that is, resolving their uncertainty would be most valuable for this case study. From a societal perspective, however, productivity costs got priority, while these were by their very nature ignored from a health care perspective.

The current case study could be illustrative for many other mental disorders: often productivity costs represent a relatively large part of the disease burden, and they are also often relatively uncertain due to a lack of data. It is obvious that when the societal perspective is relevant for the decision maker, a VOI from a health care perspective may lead to erroneous priorities for further research, especially in the presence of large and uncertain productivity costs.

Comparing the cost-effectiveness results from a societal perspective to a health care perspective as required by most guidelines recommending a societal perspective indicates that including societal costs in the analyses may significantly affect the outcomes and even change the decisions. The changes occur regarding not only the acceptability of the intervention but also priorities for further research and VOI. According to the cost-effectiveness acceptability curves (Fig. 2), for very low willingness-to-pay thresholds, from a health care perspective rejecting the intervention seems to be the most reasonable decision. From a societal perspective, however, for low thresholds, accepting the intervention has a fair chance of being cost-effective.

To have an estimation of the EVPI, we look at the graphs at the unofficial Dutch thresholds for preventive interventions of 20,000 €/QALY [34]. This threshold was first mentioned in a health care perspective setting [35]. It has also been used, however, for analyses in a societal perspective [34]. At the threshold of 20,000 €/QALY, the global EVPIs had a value of about 42 and 32 million euros from societal and health care perspectives, respectively, both indicating that it would be worthwhile to gather more information.

Hence, using an invalid perspective could lead to unrealistic importance attached to additional research, depending on the actual threshold value. As mentioned in the “Results” section, however, considering the same threshold for both perspectives is not very practical. In real-world decisions, threshold values change on the basis of the perspective chosen. From a societal perspective, threshold values should reflect the consumption value of health, while from a health care perspective they would reflect the marginal value of health provided for by a publicly financed health care system, which are not necessarily the same. Opinions differ, however, on this issue [14,36]. Meanwhile, it is not clear how large the difference between the two thresholds

should be. In applications, similar threshold values are sometimes mentioned in studies applying a societal perspective as well as studies using a health care perspective. For instance, as mentioned before, the unofficial Dutch threshold of 20,000 €/QALY has been used in both health care and societal perspectives, indicating the difficulties in understanding the relationship between perspective and threshold in many decision contexts.

We chose to illustrate our results in graphs with a single threshold on the x-axis. If the actual thresholds were larger from a societal perspective (following the reasoning in Claxton et al. [14]), then a figure that compares both perspectives should use two different scales on the x-axis, effectively shifting the societal perspective graph to the left. This implies that the differences between the societal and health care perspectives in the value of the global EVPI decrease. It is obvious that the only way to reach a precise comparison between the VOI from the two perspectives is to know the exact willingness-to-pay threshold considering each perspective.

Using a health care perspective, VOI analysis informs decision makers about allocating funding for actual interventions and research that basically can be considered as originating from the same health care budget. All costs and savings hence refer to the same budget and decision maker, even if in reality earmarking and separate budgets will be present. Using a societal perspective, however, this may no longer hold. For instance, savings in productivity costs will accrue to employers, not to health care decision makers. In recent years, this has led to discussions on how the costs of interventions and research must be sponsored when a societal perspective is considered. Debates are mostly focused on public health interventions, in which the impacts are often wide-ranging. Costs and benefits associated with an intervention aiming at public health, such as the depression prevention case, will fall on many sectors within the society [37]. Some authors just assume that when a societal perspective is taken, the society pays for health care interventions through a single payer system and also pays for research projects for reducing uncertainties through government or private donation-based agencies [38]. Weatherly et al. [37] reviewed a number of approaches that have been suggested to account for the impact of interventions across different sectors. For instance, Claxton et al. [39] introduce a multisectoral societal decision-making approach to evaluate costs and benefits that fall on different sectors of the economy. Smith et al. [40] also demonstrate the value of using a macroeconomic approach to modeling a major health problem, using the context of antimicrobial resistance and applying general equilibrium analysis. Following Willan and Pinto [38], it seems valid to argue that a societal perspective implies that resources can—in principle—be transferred from one part of the economy to the other and the extended Pareto criterion may be applied to decide whether an intervention or additional research is worthwhile. Hence, in the presence of uncertainty, VOI analysis will inform whether additional research is potentially worthwhile from a societal point of view to support better future decision making, independent of who is going to pay or gain from this research.

To conclude, our results underlined the need for carefully choosing the relevant perspective for the decision problem at hand, also in VOI analyses, to avoid erroneous choice of research priorities.

Source of financial support: The research reported in this manuscript has been financially supported by the Dutch Ministry of Health as a part of the Dutch National Institute for Public Health and the Environment (RIVM) strategic research. RIVM is an independent research institution with full freedom of research and publication.

## REFERENCES

- [1] Raiffa H. *Decision Analysis: Introductory Lectures on Choices under Uncertainty*. New York: Random House, 1968.
- [2] Yokota F, Thompson KM. Value of information literature analysis: a review of applications in health risk management. *Med Decis Making* 2004;24:287–98.
- [3] Claxton K. The irrelevance of inference: a decision-making approach to the stochastic evaluation of health care technologies. *J Health Econ* 1999;8:341–64.
- [4] Black C, Clar C, Henderson R, et al. The clinical effectiveness of glucosamine and chondroitin supplements in slowing or arresting progression of osteoarthritis of the knee: a systematic review and economic evaluation. *Health Technol Assess* 2009;13:1–148.
- [5] Bojke L, Claxton K, Sculpher M, et al. Identifying research priorities: the value of information associated with repeat screening for age-related macular degeneration. *Med Decis Making* 2008;28:33–43.
- [6] Claxton K, Sculpher MJ. Using value of information analysis to prioritise health research: some lessons from recent UK Experience. *Pharmacoeconomics* 2006;24:1055–68.
- [7] Fox M, Mealing S, Anderson R, et al. The clinical effectiveness and cost-effectiveness of cardiac resynchronisation (biventricular pacing) for heart failure: systematic review and economic model. *Health Technol Assess* 2007;11:iii–iv, ix–248.
- [8] Hassan C, Pickhardt PJ, Giulio ED, et al. Value-of-information analysis to guide future research in the management of the colorectal malignant polyp. *Dis Colon Rectum* 2010;53:135–42.
- [9] Rojnik K, Naversnik K. Gaussian process metamodeling in Bayesian value of information analysis: a case of the complex health economic model for breast cancer screening. *Value Health* 2008;11:240–50.
- [10] Smits M, Dippel DWJ, Nederkoorn PJ, et al. Minor head injury: CT-based strategies for management—a cost-effectiveness analysis. *Radiology* 2010;254:532–40.
- [11] Wailoo AJ, Sutton AJ, Cooper NJ, et al. Cost-effectiveness and value of information analyses of neuraminidase inhibitors for the treatment of influenza. *Value Health* 2008;11:160–71.
- [12] Welton NJ, Ades AE, Caldwell DM, et al. Research prioritization based on expected value of partial perfect information: a case-study on interventions to increase uptake of breast cancer screening. *J Roy Stat Soc* 2008;171(pt 4):807–41.
- [13] Wilson E, Gurusamy K, Gluud C, et al. Cost-utility and value-of-information analysis of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. *Br J Surg* 2010;97:210–9.
- [14] Claxton K, Walker S, Palmer S, et al. *Appropriate perspectives for health care decisions*. CHE Research Paper University of York: Centre for Health Economics, 2010:54.
- [15] London: National Institute for Health and Clinical Excellence, 2009.
- [16] Spronk S, Bosch JL, Ryjewski C, et al. Cost-effectiveness of new cardiac and vascular rehabilitation strategies for patients with coronary artery disease. *PLoS One* 2008;3:e3883.
- [17] Galani C, Al M, Schneider H, et al. Uncertainty in decision-making: value of additional information in the cost-effectiveness of lifestyle intervention in overweight and obese people. *Value Health* 2008;11:424–34.
- [18] Dewa CS, McDaid D, Ettner SL. An international perspective on worker mental health problems: who bears the burden and how are costs addressed? *Can J Psychiatry* 2007;52:346–56.
- [19] Kuijshaar ME, Barendregt J, Vos T, et al. Lifetime prevalence estimates of major depression: an indirect estimation method and a quantification of recall bias. *Eur J Epidemiol* 2005;20:103–11.
- [20] Mykletun A, Bjerkeset O, Overland S, et al. Levels of anxiety and depression as predictors of mortality: the HUNT study. *Br J Psychiatry* 2009;195:118–25.
- [21] Smit F, Willemse G, Koopmanschap M, et al. Cost-effectiveness of preventing depression in primary care patients: randomised trial. *Br J Psychiatry* 2006;188:330–6.
- [22] Krol M, Papenburg J, Koopmanschap M, et al. Do productivity costs matter? The impact of including productivity costs on the incremental costs of interventions targeted at depressive disorders. *Pharmacoeconomics* 2011;29:601–9.
- [23] Van den Berg M, Smit F, Vos T, et al. Cost-effectiveness of opportunistic screening and minimal contact psychotherapy to prevent depression in primary care patients. *PLoS One* 2011;6:e22884.
- [24] Vos T, Corry J, Haby MM, et al. Cost-effectiveness of cognitive-behavioural therapy and drug interventions for major depression. *Aust N Z J Psychiatry* 2005;39:683–92.
- [25] Richtlijnen voor farmaco-economisch onderzoek, geactualiseerde versie Available from: [www.cvz.nl](http://www.cvz.nl). [Accessed March 11, 2010].



- 
- [26] Willemse G, Smit F, Cuijpers P, et al. Minimal-contact psychotherapy for sub-threshold depression in primary care: randomised trial. *Br J Psychiatry* 2004;185:416–21.
  - [27] Kessler RC, Zhao S, Blazer DG, et al. Prevalence, correlates, and course of minor depression and major depression in the National Comorbidity Survey. *J Affect Disorders* 1997;45:19–30.
  - [28] Cuijpers P, Smit F. Subthreshold depression as a risk indicator for major depressive disorder: a systematic review of prospective studies. *Acta Psychiatr Scand* 2004;109:325–31.
  - [29] Bosmans JE, Brook OH, VanHout HP, et al. Cost effectiveness of a pharmacy-based coaching programme to improve adherence to antidepressants. *Pharmacoeconomics* 2007;25:25–37.
  - [30] Stant AD, TenVergert EM, DenBoer PC, et al. Cost-effectiveness of cognitive self-therapy in patients with depression and anxiety disorders. *Acta Psychiatr Scand* 2008;117:57–66.
  - [31] VanRooijen LH, VanStraten A, Al M, et al. Cost-utility of brief psychological treatment for depression and anxiety. *Br J Psychiatry* 2006;188:323–9.
  - [32] Briggs A, Claxton K, Sculpher M. *Decision Modelling for Health Economic Evaluation*. Oxford: Oxford University Press, 2006.
  - [33] Oakley JE, Brennan A, Tappenden P, et al. Simulation sample sizes for Monte Carlo partial EVPI calculations. *J Health Econ* 2010;29:468–77.
  - [34] van den Berg M, DeWit GA, Vijgen SM, et al. Cost-effectiveness of prevention: opportunities for public health policy in the Netherlands. *Ned Tijdschr Geneesk* 2008;152:1329–34.
  - [35] Casparie AF, VanHout BA, Simoons ML. Guidelines and costs. *Ned Tijdschr Geneesk* 1998;142:2075–7.
  - [36] Jönsson B. Ten arguments for a societal perspective in the economic evaluation of medical innovations. *Eur J Health Econ* 2009;10:357–9.
  - [37] Weatherly H, Drummond M, Claxton K, et al. Methods for assessing the cost-effectiveness of public health interventions: key challenges and recommendations. *Health Policy* 2009;93:85–92.
  - [38] Willan AR, Pinto EM. The value of information and optimal clinical trial design. *Stat Med* 2005;24:1791–806.
  - [39] York: Centre for Health Economics, 2007.
  - [40] Smith RD, Yago M, Millar M, et al. Assessing the macroeconomic impact of a healthcare problem: the application of computable general equilibrium analysis to antimicrobial resistance. *J Health Econ* 2005;24:1055–75.